IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT	:	Richard, Robert
SERIAL NO.	:	09/879,216
FILED	:	June 13, 2001
FOR	:	SUPERCRITICAL FLUIDS TO INFUSE THERAPEUTIC ON MEDICAL DEVICE
GROUP ART UNIT	:	1762
Examiner	:	J. KOLB MICHENER

ASSISTANT COMMISSIONER FOR PATENTS
Washington, D.C. 20231

DECLARATION OF ROBERT E. RICHARD

I, Robert E. Richard, declare as follows:

1. I am the inventor of the above-referenced patent application currently pending before the United States Patent and Trademark Office. I am informed that the application currently contains claims 1-20, of which claims 16-20 stand withdrawn from consideration following an election/restriction requirement. I am further informed that claims 1-2, 4-8, 10-12 and 14-15 stand rejected as anticipated under 35 U.S.C. § 102(e) by U.S. Patent Application Ser. No. 09/836,161 (U.S. Patent Application Publication No. U.S. 2002/0051845 A1) by Mehta, *et al.* ("Mehta"), which has a filing date of April 17, 2001, and that claims 3, 7, 9 and 13 stand rejected as obvious in view of Mehta.

2. I conceived of the subject matter recited in the pending claims of this application prior to April 17, 2001. Evidence of this fact is shown in the attached Exhibit A, which was written in 2000. Exhibit A is the invention disclosure document submitted to the Boston Scientific Patent Review Board that describes concepts that lead to the filing of the invention "SUPERCRITICAL FLUIDS TO INFUSE THERAPEUTIC ON MEDICAL DEVICE."

3. Exhibit A illustrates that conception of the subject matter recited in the pending claims had occurred by 2000. For example, the date listed for the earliest known documentation of the idea is in 2000. Further, I exercised diligence in reducing the invention to practice, as substantially the entire focus of my employment at SCIMED Life Systems, Inc. during this time was devoted to development of this invention. Reduction to practice of

the claimed subject matter occurred by 2000, as indicated by the reference in Exhibit A to a bench test in 2000 that established the invention would work for its intended purpose beyond the probability of failure.

4. All my work to conceive and reduce to practice the subject matter claimed in the above-referenced application was done in SCIMED Life Systems, Inc.'s Massachusetts facilities.

7. As shown above, I had conceived and reduced to practice the subject matter claimed in the pending application earlier than April 17, 2001.

I, Robert E. Richard, declare that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true and that all statements made herein are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. § 1001) and may jeopardize the validity of the application or any patent issuing thereon.

Dated: June 4, 2003

Robert E. Richard

Dmy

00-D0734

Boston Scientific Corporation

IDEA DISCLOSURE

Title of Idea: **Process to Prepare Polymer/TherapeuticAgent Coated Stents**

BSC Division/Technology: Molecular Interventions

Date you begin filling out this form: [redacted]00

Key words for search: Stent coatings, drugs, therapeutic agents, SIBS

Innovator(s):

Name (First, MI, Last) (As you like it to appear on a Patent): Robert E. Richard
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Home Phone No.: 508-883-5176
Signature: Robert E Richard **Date:** [redacted]-00

Name (First, MI, Last) (As you like it to appear on a Patent):
Work Location: **Work Phone Ext.:**
Home Address: **State:** **Zip:** **Country:**
Home Phone No.:
Signature: **Date:**

Name (First, MI, Last) (As you like it to appear on a Patent):
Work Location: **Work Phone Ext.:**
Home Address: **State:** **Zip:** **Country:**
Home Phone No.:
Signature: **Date:**

Name (First, MI, Last) (As you like it to appear on a Patent):
Work Location: **Work Phone Ext.:**
Home Address: **State:** **Zip:** **Country:**
Home Phone No.:
Signature: **Date:**

Witnessed Signature: [signature] **Date** [redacted]00
Position: Sr. Scientist **Work Phone Ext.:** 8344

Witnessed Signature: [signature] **Date** [redacted]00
Position: Sr. Engineer **Work Phone Ext.:** 5243

Boston Scientific Corporation

I. Description of Idea

1. **Briefly describe the current technology, devices, methods, etc. that relates to your idea and any disadvantages of the current technology. (Please attach any copies of articles, patents, drawings, pictures, brochures, presentations, instructions for use, etc. describing the current technology.)**

This disclosure relates to processes used to make drug (or other active agents like genes, DNA, proteins, etc.) eluting stents. Current technology to produce such devices involves operations such as spraying a solution of polymer plus drug onto the surface of a stent. A specific example of such a system is the paclitaxel(PTx)/SIBS [SIBS = poly(styrene-isobutylene-styrene)] coated stent. This technology involves dissolving PTx and SIBS in an organic solvent mixture (toluene and tetrahydrofuran) and spraying the solution onto stents. The disadvantages to this system are that: (1) only a fraction of the PTx is eluted from the stent in practice, with the remainder probably locked with the polymer permanantly. (2) Because the PTx is a highly potent drug, the spraying operation is carried out in an expensive glove box apparatus. (3) The stents need to be precisely coated to get the required drug loading and the operation is currently slow.

2. **How does your idea address the disadvantages of the current technology? What problems are solved by your idea? What is different from the current technology? What are the advantages of your idea?**

The concept of swelling the polymer carrier coated onto a stent in a solution of drug in supercritical fluid could allow more of the drug to be eluted from the coating in situ. This would allow a more accurate dose to be administered and would also be more cost effective since the drug is very expensive and incorporating drug that never elutes from the stent is impractical.

If only the polymer carrier, for example SIBS, was to be spray coated onto the stent the conditions would not need to be as rigorous or slow , since accuracy required for the current operation would not be needed. Also since the drug is introduced in a second step (SCF swelling step) a large number of stents could potentially be impregnated with drug at the same time (and with a more reproducible and precise dose from unit to unit). Additionally, since the unsed drug would remain in the SCF and could be easily reclaimed. This operation would also result in less wasted drug than a spraying operation where a significant portion of the drug spray does not land on the stent).

3. **Describe in detail the construction and operation of your device or method, specifically pointing out advantages of your idea (e.g. speed, simplicity, repeatability, accuracy, lower cost, etc.) Attach drawings as appendices and refer to those drawings in the text. A good technique is to first describe the structure of the device and then its operation.**

The preferred process would involve placing a number of stents that had been precoated with a polymer carrier only (such as SIBS) in a chamber into which SCF could be generated. The SCF would be chosen such that the drug was readily soluble in it (since paclitaxel is soluble in supercritical carbon dioxide it would be a good choice for this drug). The SCF would also need to swell the polymer carrier sufficiently to allow the drug to imbibe into it (since it has been determined that SIBS is swellable in supercritical carbon dioxide it would be a good choice for this polymer carrier).

The advantages of this system are: (1) speed of operation since a number of stents could be impregnated with drug simultaneously,(2)accuracy of drug dose since a large number of units are produced together and so that process variation would be reduced, (3) lower cost since any drug not imbibed into the polymer could be readily reclaimed and reused for subsequent process runs, (4) the ability to better control the percentage of drug that ultimately elutes from the stent.

4. **Alternatives: Describe any alternative designs, methods f construction r operation or manufacturing of the above device or method. For example, are there alternative materials that may be cheaper or that may provide different features such as stiffness? Are there other products or devices that may incorporate the idea? What other features might the idea incorporate? Put yourself in the competitor's shoes... How w uld you take advantage of this idea but avoid the device or method?**

The primary product system addressed by this disclosure is the SIBS/pTx coated stent. Variations could include any agent (DNA, genes, proteins, or any other therapeutic agent like NO, enzymes, etc..) impregnated into any substrate which swells or can be permeated by a supercritical fluid. Altghough the present disclosure used supercritical carbon dioxide, other SCFs could be used depending on the chemical nature of the carrier or the drug

5. **What BSC products are affected? What competitor products are affected?**

The primary product affected would be the paclitaxel eluting stent that is currently being developed. Other products that could potentially benefit from this technology would include PCTA balloons or any other product currently used to deliver a therapeutic agent to a specific site in the body.

6. **Will the idea be manufactured outside the US? If so, where? Please list any foreign countries you believe BSC should seek patent protection in and why. For example, a competitor manufactures in France or the market potential is highest in Japan.**

The product could be manufactured in Ireland. Patent protection in Europe and Japan should be considered

II. General Information

1. **Documentation of Idea:**

   a. **Date of earliest known documentation of idea: (Please attach a copy if available.)** [redacted]-00
   Lab Notebook No.: 391 **Page No(s).:** 1
   If different, date of first known drawings: _____
   b. **Who has custody of drawings?:** _____
   c. **Date of first known internal disclosure:** [redacted]-00
   To whom: Marlene Schwarz

2. **Prototype:**

   a. **Start date of first known prototype/model build:** **(add any description of the first or other prototypes that may be helpful)** TBD
   b. **Date of first known test of idea: (add any description of test results that may be helpful)** [redacted]-00
   Bench, Animal or Clinical?: Bench
   c. **Please list any witnesses who saw the prototype.:** Kara Brennan, Phasex Corp.

3. **Project phase:**

   a. **What is the current project phase (concept, development or scale-up?):** Concept
   b. **Product to be released:** [redacted] **Release date:** _____
   c. **Engineering Project Number:** 101404

4. **Disclosure outside of BSC:**

   a. **Has the idea been disclosed outside of BSC?:** yes
   b. **If NO:**
   Is a future disclosure planned?: _____ **Where?:** _____ **When?:** _____
   (If less than 2 months away, please notify the on-site patent representative immediately.)
   c. **If YES:**
   Was the disclosure written or oral?: Both
   To whom was the disclosure made and why?: [redacted] of Phasex Corp., They possess the SCF technology needed to test the concept
   By whom?: Bob Richard **Is a written confidentiality agreement (CDA) in place?:** Yes

5. **Prototype External to BSC:**

   a. **Has a prototype or model been used or shipped external to BSC?:** No
   b. **Has the idea been incorporated in a commercially released product?:** No
   c. **If NO:**
   When is a prototype expected to be used or shipped external to BSC?: 1Q01
   When is a product expected to be commercially released?: TBD
   (If less than 2 months away, please notify the on-site patent representative immediately.)

6. **Please list any potentially relevant publications, presentations, patents or patent applications or other descriptions of which you are aware:**

   None

7. **Name any key physicians who might be r are interested in the idea.**

[illegible] USE OF SUPERCRITICAL FLUIDS Project No.
TITLE TO COAT [illegible] DRUGS/CARRIERS ONTO STENTS Book No.

From Page No. [redacted] 2000

CURRENTLY A POLYMER/SOLVENT/DRUG SOLUTION IS SPRAYED ONTO STENTS TO PRODUCE A STENT WHICH DELIVERS DRUGS TO A VESSEL AFTER DEPLOYMENT. A CURRENT EXAMPLE IS THE PACLITAXEL/SIBS COATING. THE DISADVANTAGE TO COATING FROM AN AN ORGANIC SOLENT, WHICH IS THE CURRENT PRACTICE, IS THAT FLAMABLE AND TOXIC VAPORS ARE PRODUCED, WHICH HAVE TO BE CONTROLLED AND CONTAINED. ALSO, THE SPRAY THAT DOES NOT DEPOSIT ON THE DEVICE IS WASTED AND DIFFICULT TO RECYCLE. THE CONCEPT OF USING A SUPERCRITICAL FLUID (SCF) TO REPLACE THE SOLVENT HAS A NUMBER OF ADVANTAGE INCLUDING:

(1) SCF CAN BE EASILY CONTAINED IN A CLOSED SYSTEM AND IS EASILY RECYCLED.

(2) WHEN THE DRUG AND CARRIER CAN BOTH BE DISSOLVE IN THE SCF IT MAY BE POSSIBLE TO EMERSE THE STENTS IN THIS SCF SOLUTION AND ESSENTIALLY DIP COAT THE STENTS. THE AMOUNT DEPOSITED WOULD BE CONTROLLED BY THE CONCENTRATION OF THE POLYMER AND DRUG IN THE SOLUTION.

THIS TECHNOLOGY COULD ALSO BE USED IN A DIFFERENT WAY SUCH THAT THE CARRIER POLYMER COULD FIRST BE COATED ALONE ONTO A STENT USING SCF OR SOME OTHER APPROACH AND THEN THE POLYMER COATED STENT COULD BE CONTACTED WITH A SCF THAT SWELLS BUT DOES NO DISSOLVE THE POLYMER. IF THE DRUG IS DISSOLVE IN THIS SCF IT COULD BE IMPREGNATED INTO THE POLYMER COATING. ANOTHER OPTION COULD BE TO CROSSLINK THE POLYMER THAT IS COATED ONTO THE STENT (FOR EXAMPLE BY RADIATION EXPOSURE) AND THEN SWELL IT IN THE SCF WHICH CONTAINS THE DRUG

To Page No.

Witnessed & Understood by me,	Date	Invented by	Date
		Recorded by [redacted]	[redacted] 04

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Project No.

TITLE SCF AS PROCESS FOR SIBS/DRUG/AGENTS Book No.

From Page No. 1

FILMS OF SIBS WERE SUPPLIED TO PHASEX CORP TO ALLOW THEM TO INVESTIGATE THE FEASIBILITY OF USING SUPERCRITICAL FLUID (SCF) TO FACILITATE THE PRODUCTION OF COATINGS OF SIBS ONTO STENTS AS WELL AS A VEHICLE TO INTRODUCE AGENTS SPECIFICALLY PACLITAXEL IN THIS CASE INTO A SIBS COATING. AFTER TREATING THE FILMS OF SIBS A PRELIMINARY REPORT WAS WRITTEN WITH THEIR FINDINGS (SEE P 8-9). IT WAS determined THAT Supercritical CO_2 does influence SIBS BY CAUSING IT TO SWELL up to 100%, depending on conditions. In addition The physical appearance of the films was visibly altered in That The films changed from clear to white in color, and This effect was attributed by Phasex to gas bubble nucleation. To investigate more closely, The treated films were submitted to ANALYTICAL for microscopic evaluation to determine The change in morphology as a result of The SCF treatment.

As a result of The findings That SCF CO_2 will swell The SIBS AND knowing That PACLITAXEL IS soluble in SC-CO_2 The next step in The project will be to expose films of SIBS and/or SIBS coated stents with a SC CO_2 solution of PACLITAXEL to see if The drug can be impibed into THE SIBS as a result of The SCF induced swelling

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Witnessed & Understood by me,	Date	Invented by	Date
		Recorded by [redacted]	[redacted] 00